REMARKS

The specification has been revised to include reference to, and claim to priority from, an earlier filed application filed under the Patent Cooperation Treaty (PCT).

Claims 1-23 are pending in the application. The claims have been revised to use alternate terminology to encompass the same subject matter and to better tailor the claims to currently contemplated commercial embodiments of the invention.

Support for revised claim 1 is found at least on pages 22, 26, and 30-32 of the instant specification. Support for "solid tumor" is found at least in claim 19 and on pages 22 and 30-32 of the instant specification.

No new matter has been introduced, and entry of the above revised claims is respectfully requested.

Specification-Priority

The Examiner states that for benefit of priority claims under 35 U.S.C. § 120, 121 or 365(c), a specific reference to the earlier filed application must be included in the first sentence(s) of the specification following the title. Applicants point out that the instant application is a national phase application filed under 35 U.S.C. §371 of PCT/KR05/00075, filed January 10, 2005. Accordingly, the appropriate cross-reference information has been inserted into the specification as provided above to comply with the standard.

Alleged Rejection Under 35 U.S.C. § 101

Claims 1-23 have been rejected under 35 U.S.C. § 101 as allegedly encompassing non-statutory subject matter. Applicants have carefully reviewed the statement of the rejection and the revised claims as presented above. Reconsideration and withdrawal of this rejection is respectfully requested because claim 1 has been revised to be directed to a pharmaceutical composition for treating a solid tumor or metastasis thereof containing a gene carrier or cells harboring a gene encoding a recombinant protein consisting of human apolipoprotein (a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) as an effective ingredient. Because the cells featured in the claim harbor a gene encoding a *recombinant* protein, naturally occurring cells as they occur in a human being or a human being *per se* are not within the scope of the claim. Therefore,

Applicants respectfully submit that this rejection is not applicable to the revised claims, and so this rejection may be properly withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-23 have been rejected as allegedly non-enabled by the present specification. Applicants respectfully traverse this rejection because no *prima facie* case of non-enablement is present. Reconsideration and withdrawal of the rejection are respectfully requested.

As an initial matter, Applicants point out that the instant rejection is in conflict with the alleged obviousness-type double patenting rejection addressed below. The obviousness-type double patenting rejection asserts that, based on claims 12-14 and 20 of U.S. Patent Application 10/162,817, it would have been obvious for a skilled person in the art to make and use the subject matter of claims 18-20 across their full scope. But the instant rejection asserts that the present application does not enable the same skilled person to make and use the subject matter of claims 18-20 in a manner commensurate with the scope of the claims. Applicants respectfully submit that these two positions are mutually exclusive and so inconsistent when alleged together. Therefore, it is improper for both rejections to be made against the same claims to place Applicants in a "squeeze" between allegations of obviousness and non-enablement. Correction of this improper situation is respectfully requested.

Additionally, Applicants point out the well established standard that an application must be taken as presumptively enabling unless there is objective reason to doubt the statements contained therein (see MPEP 2164.04 and the case decisions cited therein, such as *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)). This presumption is present before any "determination of enablement" is to occur under the *In re Wands* factors as cited in the instant rejection. Applicants submit that no objective reason has been provided to doubt the presumption of enablement in the pending claims.

The lack of an objective reason is clearly evident with respect to claims 1-17, 22, and 23. These claims are directed to compositions which are not limited to "gene therapy" as alleged in the instant rejection. Therefore, there must be a separate demonstration of undue experimentation as necessary to make and use these compositions. But the instant rejection recognizes the ability to treat tumors by direct injection with the claimed compositions. This is

consistent with the lack of undue experimentation to make and use the subject matter of claims 1-17, 22, and 23. Additionally, this recognition supports the presumption of enablement for these claims. Accordingly, the instant rejection is misplaced against these claims and may be properly withdrawn.

With respect to claims 18-21, Applicants point out that claims 18-20 feature "parenteral administration" while claim 21 features "injecting cells". Therefore, and contrary to the allegations in the instant rejection, the claims do not encompass "any method of administration". Additionally, and with respect to claim 21, the injection of cells reflects the use of methods such as *ex vivo* modification of cells followed by their return to an individual. Applicants respectfully submit that the instant rejection's focus on gene therapy comprising the administration of nucleic acid molecules or vectors shows that it is misplaced with respect to claim 21.

As for claims 18-20, Applicants submit that the instant rejection relies upon speculation and not objective evidence. For example, the cited document by Goncalves et al. and report on treatment of X-SCID patients do not provide any objective reason to doubt the presumption of enablement for parenteral administration of a "gene carrier or cells" as featured in claims 18-21. The cited document does not specifically deal with the treatment of solid tumors by parenteral administration of the compositions as claimed.

Therefore, there is no objective reason to doubt the ability to use an AAV vector and other gene carriers without undue experimentation. For example, there is no specific objective reason to doubt the ability to use linear DNA vector and plasmid DNA vector to carry a gene encoding a recombinant LK68 or LK8 protein. Various vectors for anti-angiogenic gene therapy are also exemplified in Isayeva et al. (International Journal of Oncology 25:335-343, 2004), which is submitted herewith.

Additionally, the Examiner is directed to the Declaration of Dr. Eui Cheol Jo under 37 C.F.R. § 1.132 as submitted herewith. The Declaration provides objective evidence of using naked plasmids, pcDNA/LK8 and pcDNA/LK68, without undue experimentation to produce anti-angiogenic, and so anti-solid tumor, activity. The data in the Declaration also supports the use of an AAV vector, which is representative of other vector or plasmids that express LK8 or LK68, to produce the same beneficial activity.

In light of the lack of evidence supporting the instant rejection and additional evidence supporting the presumption of enablement for the pending claims, Applicants respectfully submit that the instant rejection is misplaced and should be withdrawn.

Alleged Rejection Under 35 U.S.C. §102(b) over Trieu (1999, Biochem. Biophys. Res. Comm. 257:714-718)

Claims 1, 3-4, 6, and 16 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Trieu et al. Applicants respectfully traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Trieu et al. report that the mean microvessel density of subcutaneous LL/2 (Lewis Lung Carcinoma) tumors from apolipoprotein(a) transgenic mice was significantly lower than that of tumors from control wild type mice. Trieu et al. also report that CHO cells secreting a truncated apo(a) protein with only six kringle 4 repeats did not exhibit delayed tumor growth nor did it impair angiogenesis.

The standards for anticipation are well settled and include the requirement for a single document to disclose each and every feature of a claimed invention (see for example MPEP 2131 and the case decisions cited therein).

In the instant case, Applicants point out that the amino acid sequence of apolipoprotein(a) reported by Trieu et al., differ from the amino acid sequences of the LK68 (human apolipoprotein(a) kringle KIV9-KIV10-KV) and LK8 (human apolipoprotein(a) kringle KV) polypeptides featured in the pending claims.

Additionally, and while Trieu et al. report a possible role of full length apolipoprotein(a) on angiogenesis and cancer biology, Trieu et al. fail to disclose or suggest that LK68 or LK8 protein is useful for treatment of a solid tumor as featured in the pending claims. Moreover, Trieu et al. report that Ha6, consisting of 6 repeated kringle IVs and one kringle V failed to suppress tumor angiogenesis.

In light of the foregoing, Trieu et al. fail to disclose the instantly claimed invention, and so this rejection may be properly withdrawn.

Alleged Rejection under the Judicially Created Doctrine of Obviousness-type Double Patenting over Claims 12-14 and 20 of U.S. Application No. 10/162,817 (USPTO Pub. No. US2006/0013823A1)

Claims 18-20 have been rejected on the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 12-14 and 20 of U.S. Application No. 10/162,817. Applicants respectfully traverse this rejection because no *prima facie* case of obviousness-type double patenting is present. Reconsideration and withdrawal thereof are respectfully requested.

As an initial matter, Applicants point out that the instant rejection is in conflict with the alleged lack of enablement rejection addressed above. The instant obviousness-type double patenting rejection asserts that, based on claims 12-14 and 20 of U.S. Patent Application 10/162,817, it would have been obvious for a skilled person in the art to make and use the subject matter encompassed by claims 18-20 across their full scope. But the alleged enablement rejection addressed above asserts that the present application does not enable the same skilled person to make and use the subject matter of claims 18-20 in a manner commensurate with the scope of the claims. Again, Applicants point out that these two positions are mutually exclusive and so inconsistent when alleged together. Applicants respectfully request correction of this improper assertion of inconsistent positions.

Turning to the instant rejection, U.S. Application No. 10/162,817 discloses a method of reducing tumor growth by using a composition comprising LK8 or LK68 *protein*. In particular, claims 12-14 and 20 therein feature a method for inhibiting metastasis of cancer comprising administering a combination of a composition comprising LK8 or LK68 *protein* and radiation therapy, immunotherapy or chemotherapy to a subject. But claims 18-20 of the present application are drawn to methods featuring parenteral administration of a composition containing a gene carrier or cells harboring a *gene* encoding a recombinant protein consisting of LK68 or LK8.

For the instantly claimed subject matter to be *prima facie* obvious over the claims of the cited document, the allegation of obviousness cannot be based upon the body of the cited application (see MPEP 804II.B.1. and the case decisions cited therein). Therefore, a proper

rejection must be based only upon the claims of the cited document applied in accordance with MPEP 804II.B.

But the instant statement of the rejection improperly relies upon citations from the specification of application 10/162,817 (see paragraph bridging pages 7 and 8 in the Office Action mailed January 24, 2007). Therefore, the standards for an obviousness-type double patenting rejection have not been met, and so no *prima facie* case is present. This rejection is thus misplaced and may be properly withdrawn.

Conclusion

It is believed that the application is now in condition for allowance. Applicants request the Examiner to issue a notice of Allowance in due course. The Examiner is encouraged to contact the undersigned to further the prosecution of the present invention.

The Commissioner is authorized to charge JHK Law's Deposit Account No. **502486** for any fees required under 37 CFR §§ 1.16 and 1.17 and to credit any overpayment to said Deposit Account No. **502486**.

Respectfully submitted,

JHK Law

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